

Application No. 10/776,649  
Second Supplemental Preliminary Amendment Dated July 22, 2005

**Amendments to the Claims:**

Please cancel claims 1-4 and 7-20 and add claims 105 to 366. This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1.-104. (Cancelled)

105. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that competes for binding to human CTLA-4 with an antibody comprising the heavy chain FR1 through FR4 amino acid sequence in SEQ ID NO: 1 and the light chain FR1 through FR4 amino acid sequence in SEQ ID NO: 14, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2 and wherein said competing human monoclonal antibody comprises a light chain that utilizes a human A27 V $\kappa$  gene.

106. (New) The mammalian host cell line according to claim 105, further comprising a glutamine synthetase expression system.

107. (New) The mammalian host cell line according to claim 105, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with and IC<sub>50</sub> of 100 nM or less.

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108. (New) The mammalian host cell line according to claim 105, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

109. (New) The mammalian host cell line according to claim 105, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

110. (New) The mammalian host cell line according to claim 105, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

111. (New) The mammalian host cell line according to claim 105, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

112. (New) The mammalian host cell line according to claim 105, wherein said polynucleotide encoding said light chain of said competing human monoclonal antibody encodes an amino acid sequence having at least 95% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

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113. (New) The mammalian host cell line according to claim 105, wherein said antibody comprising the heavy chain FR1 through FR4 amino acid sequence in SEQ ID NO: 1 and the light chain FR1 through FR4 amino acid sequence in SEQ ID NO: 14 further comprises the heavy chain and light chain constant region amino acid sequences in said SEQ ID NO: 1 and SEQ ID NO: 14, respectively.

114. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that competes for binding to human CTLA-4 with the antibody produced by hybridoma 4.1.1 deposited with the A.T.C.C. under accession number \_\_\_\_\_ wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2 and wherein said competing human monoclonal antibody comprises a light chain that utilizes a human A27 V $\kappa$  gene

115. (New) The mammalian host cell line according to claim 114, further comprising a glutamine synthetase expression system.

116. (New) The mammalian host cell line according to claim 114, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with and IC<sub>50</sub> of 100 nM or less.

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117. (New) The mammalian host cell line according to claim 114, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

118. (New) The mammalian host cell line according to claim 114, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

119. (New) The mammalian host cell line according to claim 114, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

120. (New) The mammalian host cell line according to claim 114, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

121. (New) The mammalian host cell line according to claim 114, wherein said polynucleotide encoding said light chain of said competing human monoclonal antibody encodes an amino acid sequence having at least 95% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

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122. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that competes for binding to human CTLA-4 with antibody 4.1.1 deposited with the A.T.C.C. under accession number \_\_\_\_\_, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2, and wherein the heavy chain of said competing human monoclonal antibody comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence encoded by a human DP50 gene, and the light chain comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

123. The mammalian host cell line according to claim 122, further comprising a glutamine synthetase expression system.

124. (New) The mammalian host cell line according to claim 122, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an  $IC_{50}$  of 100 nM or less.

125. (New) The mammalian host cell line according to claim 122, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

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126. (New) The mammalian host cell line according to claim 122, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

127. (New) The mammalian host cell line according to claim 122, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

128. (New) The mammalian host cell line according to claim 122, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

129. (New) The mammalian host cell line according to claim 122, wherein the light chain of said competing human monoclonal antibody comprises an amino sequence having at least 95% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

130. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that competes for binding to human CTLA-4 with the antibody produced by hybridoma 4.1.1 deposited with the A.T.C.C. under accession number \_\_\_\_\_ wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to

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human B7-1 and human B7-2, and wherein the polynucleotide encoding said heavy chain comprises a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence of a human DP50 gene, and the polynucleotide encoding said light chain comprises a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene.

131. The mammalian host cell line according to claim 130 further comprising a glutamine synthetase expression system.

132. (New) The mammalian host cell line according to claim 130, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an  $IC_{50}$  of 100 nM or less.

133. (New) The mammalian host cell line according to claim 130, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

134. (New) The mammalian host cell line according to claim 130, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

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135. (New) The mammalian host cell line according to claim 130, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

136. (New) The mammalian host cell line according to claim 130, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

137. (New) The mammalian host cell line according to claim 130, wherein the polynucleotide encoding said antibody heavy chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human DP50 gene.

138. (New) The mammalian host cell line according to claim 130, wherein the polynucleotide encoding said antibody light chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene.

139. (New) The mammalian host cell line according to claim 130, wherein the polynucleotide encoding said antibody heavy chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human DP50 gene, and the polynucleotide



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encoding said light chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene?

140. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that competes for binding to human CTLA-4 with an antibody that comprises the heavy chain FR1 through FR4 amino acid sequence in SEQ ID NO: 1 and the light chain FR1 through FR4 amino acid sequence in SEQ ID NO: 14, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2, and wherein the heavy chain of said competing human monoclonal antibody comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence encoded by a human DP50 gene, and the light chain comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

141. The mammalian host cell line according to claim 140 further comprising a glutamine synthetase expression system.

142. (New) The mammalian host cell line according to claim 140, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with and IC<sub>50</sub> of 100 nM or less.

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143. (New) The mammalian host cell line according to claim 140, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

144. (New) The mammalian host cell line according to claim 140, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

145. (New) The mammalian host cell line according to claim 140, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

146. (New) The mammalian host cell line according to claim 142, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

147. (New) The mammalian host cell line according to claim 140, wherein said competing human monoclonal antibody comprises a light chain comprising an amino sequence having at least 95% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

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148. (New) The mammalian host cell line according to claim 140, wherein said antibody comprising the heavy chain FR1 through FR4 amino acid sequence in SEQ ID NO: 1 and the light chain FR1 through FR4 amino acid sequence in SEQ ID NO: 14 further comprises the heavy chain and light chain constant region amino acid sequences in said SEQ ID NO: 1 and SEQ ID NO: 14, respectively.

149. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that competes for binding to human CTLA-4 with the antibody produced by hybridoma 4.1.1 deposited with the A.T.C.C. under accession number \_\_\_\_\_, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2, and wherein the polynucleotide encoding the heavy chain of said competing human monoclonal antibody comprises a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence in SEQ ID NO: 27 that encodes the heavy chain FR1 through FR4 amino acid sequence, and the polynucleotides encoding the light chain of said competing human monoclonal antibody comprise a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

150. The mammalian host cell line according to claim 149 further comprising a glutamine synthetase expression system.

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151. (New) The mammalian host cell line according to claim 149, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an  $IC_{50}$  of 100 nM or less.

152. (New) The mammalian host cell line according to claim 149, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

153. (New) The mammalian host cell line according to claim 149, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

154. (New) The mammalian host cell line according to claim 149, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

155. (New) The mammalian host cell line according to claim 149, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

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156. (New) The mammalian host cell line according to claim 149, wherein the polynucleotide encoding said antibody heavy chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 27 that encodes the heavy chain FR1 through FR4 amino acid sequence .

157. (New) The mammalian host cell line according to claim 149, wherein the polynucleotide encoding said antibody light chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence .

158. (New) The mammalian host cell line according to claim 149, wherein the polynucleotide encoding said heavy chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 27 that encodes the heavy chain FR1 through FR4 amino acid sequence, and the polynucleotide encoding said light chain comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

159. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that specifically binds to CTLA-4, wherein said antibody comprises a light chain that utilizes a human A27 V $\kappa$  gene and inhibits binding of human CTLA-4 to human B7-1 and human B7-2, further wherein the polynucleotide encoding

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said heavy chain of said antibody encode an amino acid sequence having at least 90% sequence identity to the amino acid sequence encoded by a human DP50 gene.

160. The mammalian host cell line according to claim 159 further comprising a glutamine synthetase expression system.

161. (New) The mammalian host cell line according to claim 159, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an  $IC_{50}$  of 100 nM or less.

162. (New) The mammalian host cell line according to claim 159, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

163. (New) The mammalian host cell line according to claim 159, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

164. (New) The mammalian host cell line according to claim 159, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

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165. (New) The mammalian host cell line according to claim 159, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.
166. (New) The mammalian host cell line according to claim 159, wherein said polynucleotide encoding said light chain of said antibody encodes an amino acid sequence having at least 95% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.
167. (New) The mammalian host cell line according to claim 159, wherein the light chain of said antibody comprises the FR1 through FR4 amino acid sequence in SEQ ID NO: 14 and the heavy chain of said antibody comprises the FR1 through FR4 amino acid sequence in SEQ ID NO: 1.
168. (New) A mammalian host cell line comprising polynucleotides encoding the heavy and light chains of a human monoclonal antibody that specifically binds to CTLA-4, wherein said antibody possesses a selectivity for human CTLA-4 over human CD28, human B7-2, human CD44, and hIgG1 of greater than 100:1 and inhibits binding between human CTLA-4 and human B7-2 with an  $IC_{50}$  of lower than 5 nM, further wherein the heavy chain of said human monoclonal antibody comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence encoded by a human DP50 gene, and the light chain comprises an amino

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acid sequence having at least 90% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

169. (New) The mammalian host cell line according to claim 168, further comprising a glutamine synthetase expression system.

170. (New) The mammalian host cell line according to claim 168, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an IC<sub>50</sub> of 5 nM or less.

171. (New) The mammalian host cell line according to claim 168, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 with an IC<sub>50</sub> of 2 nM or less.

172. (New) The mammalian host cell line according to claim 168, wherein said human monoclonal antibody inhibits binding of human CTLA-4 to human B7-2 with an IC<sub>50</sub> of 2 nM or less.



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173. (New) The mammalian host cell line of claim 168, wherein said human monoclonal antibody comprises a light chain comprising an amino sequence having at least 95% sequence identity to the amino acid sequence encoded by a human A27 V $\kappa$  gene.

174. (New) The mammalian host cell line of claim 168, further wherein the polynucleotide encoding the heavy chain of said human monoclonal antibody comprises a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence in SEQ ID NO: 27 that encodes the heavy chain FR1 through FR4 amino acid sequence, and the polynucleotides encoding the light chain of said human monoclonal antibody comprise a nucleotide sequence having at least 90% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

175. (New) The mammalian host cell line of claim 168, further wherein the polynucleotide encoding the light chain of said human monoclonal antibody comprises a nucleotide sequence encoding an amino acid sequence having at least 90% sequence identity to the light chain FR1 through FR4 amino sequence in SEQ ID NO: 14.

176. (New) The mammalian host cell line of claim 168, further wherein the polynucleotide encoding the light chain of said human monoclonal antibody comprises a nucleotide sequence encoding an amino acid sequence having at least 95% sequence identity to the light chain FR1 through FR4 amino sequence in SEQ ID NO: 14.

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177. (New) The mammalian host cell line of claim 168, further wherein the polynucleotide encoding the light chain of said human monoclonal antibody comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

178. (New) The mammalian host cell line of claim 168, further wherein the polynucleotide encoding the heavy chain of said human monoclonal antibody comprises a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 27 that encodes the heavy chain FR1 through FR4 amino acid sequence.

179. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 113 and recovering said competing human monoclonal antibody.

180. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 114 and recovering said competing human monoclonal antibody.

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181. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 115 and recovering said competing human monoclonal antibody.

182. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 119 and recovering said competing human monoclonal antibody.

183. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 121 and recovering said competing human monoclonal antibody.

184. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 122 and recovering said competing human monoclonal antibody.

185. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 123 and recovering said competing human monoclonal antibody.

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186. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 127 and recovering said competing human monoclonal antibody.

187. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 129 and recovering said competing human monoclonal antibody.

188. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 130 and recovering said competing human monoclonal antibody.

189. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 131 and recovering said competing human monoclonal antibody.

190. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 135 and recovering said competing human monoclonal antibody.

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191. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 137 and recovering said competing human monoclonal antibody.

192. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 138 and recovering said competing human monoclonal antibody.

193. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 139 and recovering said competing human monoclonal antibody.

194. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 140 and recovering said competing human monoclonal antibody.

195. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 141 and recovering said competing human monoclonal antibody.

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196. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 145 and recovering said competing human monoclonal antibody.

197. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 147 and recovering said competing human monoclonal antibody.

198. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 148 and recovering said competing human monoclonal antibody.

199. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 149 and recovering said competing human monoclonal antibody.

200. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 150 and recovering said competing human monoclonal antibody.

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201. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 153 and recovering said competing human monoclonal antibody.

202. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 156 and recovering said competing human monoclonal antibody.

203. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 157 and recovering said competing human monoclonal antibody.

204. (New) A method comprising expressing said competing human monoclonal antibody in said mammalian host cell line of claim 158 and recovering said competing human monoclonal antibody.

205. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 159 and recovering said human monoclonal antibody.

206. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 160 and recovering said human monoclonal antibody.

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207. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 164 and recovering said human monoclonal antibody.

208. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 166 and recovering said human monoclonal antibody.

209. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 1167 and recovering said human monoclonal antibody.

210. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 168 and recovering said human monoclonal antibody.

211. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 169 and recovering said human monoclonal antibody.

212. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 173 and recovering said human monoclonal antibody.

213. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 175 and recovering said human monoclonal antibody.



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214. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 176 and recovering said human monoclonal antibody.

215. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 177 and recovering said human monoclonal antibody.

216. (New) A method comprising expressing said human monoclonal antibody in said mammalian host cell line of claim 178 and recovering said human monoclonal antibody.

217. (New) The method of claim 180 further comprising contacting said competing human monoclonal antibody with protein A.

218. (New) The method of claim 180 further comprising subjecting said competing human monoclonal antibody to size exclusion chromatography.

219. (New) The method of claim 180 further comprising determining protein concentration for said competing human monoclonal antibody.

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220. (New) The method of claim 180 further comprising subjecting said competing human monoclonal antibody to N-terminal sequencing.

221. (New) The method of claim 180 further comprising testing said competing human monoclonal antibody for antigen specificity in an ELISA.

222. (New) The method of claim 184 further comprising contacting said competing human monoclonal antibody with protein A.

223. (New) The method of claim 184 further comprising subjecting said competing human monoclonal antibody to size exclusion chromatography.

224. (New) The method of claim 184 further comprising determining protein concentration for said competing human monoclonal antibody.

225. (New) The method of claim 184 further comprising subjecting said competing human monoclonal antibody to N-terminal sequencing.

226. (New) The method of claim 184 further comprising testing said competing human monoclonal antibody for antigen specificity in an ELISA.

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227. (New) The method of claim 188 further comprising contacting said competing human monoclonal antibody with protein A.
228. (New) The method of claim 188 further comprising subjecting said competing human monoclonal antibody to size exclusion chromatography.
229. (New) The method of claim 188 further comprising determining protein concentration for said competing human monoclonal antibody.
230. (New) The method of claim 188 further comprising subjecting said competing human monoclonal antibody to N-terminal sequencing.
231. (New) The method of claim 188 further comprising testing said competing human monoclonal antibody for antigen specificity in an ELISA.
232. (New) The method of claim 199 further comprising contacting said competing human monoclonal antibody with protein A.
233. (New) The method of claim 199 further comprising subjecting said competing human monoclonal antibody to size exclusion chromatography.

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234. (New) The method of claim 199 further comprising determining protein concentration for said competing human monoclonal antibody.

235. (New) The method of claim 199 further comprising subjecting said competing human monoclonal antibody to N-terminal sequencing.

236. (New) The method of claim 199 further comprising testing said competing human monoclonal antibody for antigen specificity in an ELISA.

237. (New) The method of claim 205 further comprising contacting said human monoclonal antibody with protein A.

238. (New) The method of claim 205 further comprising subjecting said human monoclonal antibody to size exclusion chromatography.

239. (New) The method of claim 205 further comprising determining protein concentration for said human monoclonal antibody.

240. (New) The method of claim 205 further comprising subjecting said human monoclonal antibody to N-terminal sequencing.

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241. (New) The method of claim 205 further comprising testing said human monoclonal antibody for antigen specificity in an ELISA.

242. (New) The method of claim 210 further comprising contacting said human monoclonal antibody with protein A.

243. (New) The method of claim 210 further comprising subjecting said human monoclonal antibody to size exclusion chromatography.

244. (New) The method of claim 210 further comprising determining protein concentration for said human monoclonal antibody.

245. (New) The method of claim 210 further comprising subjecting said human monoclonal antibody to N-terminal sequencing.

246. (New) The method of claim 210 further comprising testing said human monoclonal antibody for antigen specificity in an ELISA.

247. (New) The method of claim 180 further wherein said competing human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain that comprises a

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nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene

248. (New) The method of claim 180 further wherein said competing human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

249. (New) The method of claim 184 further wherein said competing human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain that comprise a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene

250. (New) The method of claim 184 further wherein said competing human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

251. (New) The method of claim 194 further wherein said competing human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain that comprise a

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nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene

252. (New) The method of claim 194 further wherein said competing human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

253. (New) The method of claim 205 further wherein said human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain that comprise a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene

254. (New) The method of claim 205 further wherein said human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

255. (New) The method of claim 210 further wherein said human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain that comprise a nucleotide

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sequence having at least 95% sequence identity to the nucleotide sequence of a human A27 V $\kappa$  gene

256. (New) The method of claim 210 further wherein said human monoclonal antibody is expressed using a polynucleotide encoding said antibody light chain comprising a nucleotide sequence having at least 95% sequence identity to the nucleotide sequence in SEQ ID NO: 40 that encodes the light chain FR1 through FR4 amino acid sequence.

257. (New) The mammalian host cell line according to claim 105 which is a CHO cell line.

258. (New) The mammalian host cell line according to claim 105 which is an NSO cell line.

259. (New) The mammalian host cell line according to claim 106 which is a CHO cell line.

260. (New) The mammalian host cell line according to claim 106 which is an NSO cell line.

261. (New) The mammalian host cell line according to claim 113 which is a CHO cell line.

262. (New) The mammalian host cell line according to claim 113 which is an NSO cell line.

263. (New) The mammalian host cell line according to claim 114 which is a CHO cell line.



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264. (New) The mammalian host cell line according to claim 114 which is an NSO cell line.

265. (New) The mammalian host cell line according to claim 115 which is a CHO cell line.

266. (New) The mammalian host cell line according to claim 115 which is an NSO cell line.

267. (New) The mammalian host cell line according to claim 119 which is a CHO cell line.

268. (New) The mammalian host cell line according to claim 119 which is an NSO cell line.

269. (New) The mammalian host cell line according to claim 121, which is a CHO cell line.

270. (New) The mammalian host cell line according to claim 121, which is an NSO cell line.

271. (New) The mammalian host cell line according to claim 122 which is a CHO cell line.

272. (New) The mammalian host cell line according to claim 122 which is an NSO cell line.

273. (New) The mammalian host cell line according to claim 123 which is a CHO cell line.

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274. (New) The mammalian host cell line according to claim 123 which is an NSO cell line.
275. (New) The mammalian host cell line according to claim 127 which is a CHO cell line.
276. (New) The mammalian host cell line according to claim 127 which is an NSO cell line.
277. (New) The mammalian host cell line according to claim 129 which is a CHO cell line.
278. (New) The mammalian host cell line according to claim 129 which is an NSO cell line.
279. (New) The mammalian host cell line according to claim 130 which is a CHO cell line.
280. (New) The mammalian host cell line according to claim 130 which is an NSO cell line.
281. (New) The mammalian host cell line according to claim 131 which is a CHO cell line.
282. (New) The mammalian host cell line according to claim 131 which is an NSO cell line.
283. (New) The mammalian host cell line according to claim 135 which is a CHO cell line.
284. (New) The mammalian host cell line according to claim 135 which is an NSO cell line.

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285. (New) The mammalian host cell line according to claim 137 which is a CHO cell line.

286. (New) The mammalian host cell line according to claim 137 which is an NSO cell line.

287. (New) The mammalian host cell line according to claim 138 which is a CHO cell line.

288. (New) The mammalian host cell line according to claim 138 which is an NSO cell line.

289. (New) The mammalian host cell line according to claim 139 which is a CHO cell line.

290. (New) The mammalian host cell line according to claim 139 which is an NSO cell line.

291. (New) The mammalian host cell line according to claim 140 which is a CHO cell line.

292. (New) The mammalian host cell line according to claim 140 which is an NSO cell line.

293. (New) The mammalian host cell line according to claim 141 which is a CHO cell line.

294. (New) The mammalian host cell line according to claim 141 which is an NSO cell line.

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295. (New) The mammalian host cell line according to claim 145 which is a CHO cell line.

296. (New) The mammalian host cell line according to claim 145 which is an NSO cell line.

297. (New) The mammalian host cell line according to claim 147 which is a CHO cell line.

298. (New) The mammalian host cell line according to claim 147 which is an NSO cell line.

299. (New) The mammalian host cell line according to claim 148 which is a CHO cell line.

300. (New) The mammalian host cell line according to claim 148 which is an NSO cell line.

301. (New) The mammalian host cell line according to claim 149 which is a CHO cell line.

302. (New) The mammalian host cell line according to claim 149 which is an NSO cell line.

303. (New) The mammalian host cell line according to claim 150 which is a CHO cell line.

304. (New) The mammalian host cell line according to claim 150 which is an NSO cell line.

305. (New) The mammalian host cell line according to claim 156 which is a CHO cell line.

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306. (New) The mammalian host cell line according to claim 156 which is an NSO cell line.

307. (New) The mammalian host cell line according to claim 157 which is a CHO cell line.

308. (New) The mammalian host cell line according to claim 157 which is an NSO cell line.

309. (New) The mammalian host cell line according to claim 158 which is a CHO cell line.

310. (New) The mammalian host cell line according to claim 158 which is an NSO cell line.

311. (New) The mammalian host cell line according to claim 159 which is a CHO cell line.

312. (New) The mammalian host cell line according to claim 159 which is an NSO cell line.

313. (New) The mammalian host cell line according to claim 160 which is a CHO cell line.

314. (New) The mammalian host cell line according to claim 160 which is an NSO cell line.

315. (New) The mammalian host cell line according to claim 164 which is a CHO cell line.

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316. (New) The mammalian host cell line according to claim 164 which is an NSO cell line.
317. (New) The mammalian host cell line according to claim 166 which is a CHO cell line.
318. (New) The mammalian host cell line according to claim 166 which is an NSO cell line.
319. (New) The mammalian host cell line according to claim 167 which is a CHO cell line.
320. (New) The mammalian host cell line according to claim 167 which is an NSO cell line.
321. (New) The mammalian host cell line according to claim 168 which is a CHO cell line.
322. (New) The mammalian host cell line according to claim 168 which is an NSO cell line.
323. (New) The mammalian host cell line according to claim 169 which is a CHO cell line.
324. (New) The mammalian host cell line according to claim 169 which is an NSO cell line.
325. (New) The mammalian host cell line according to claim 173 which is a CHO cell line.
326. (New) The mammalian host cell line according to claim 173 which is an NSO cell line.

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327. (New) The mammalian host cell line according to claim 175 which is a CHO cell line.

328. (New) The mammalian host cell line according to claim 175 which is an NSO cell line.

329. (New) The mammalian host cell line according to claim 176 which is a CHO cell line.

330. (New) The mammalian host cell line according to claim 176 which is an NSO cell line.

331. (New) The mammalian host cell line according to claim 177 which is a CHO cell line.

332. (New) The mammalian host cell line according to claim 177 which is an NSO cell line.

333. (New) The mammalian host cell line according to claim 178 which is a CHO cell line.

334. (New) The mammalian host cell line according to claim 178 which is an NSO cell line.

335. (New) The method of claim 180 wherein said cell line is a CHO cell line.

336. (New) The method of claim 180 wherein said cell line is an NSO cell line.

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337. (New) The method of claim 184 wherein said cell line is a CHO cell line.

338. (New) The method of claim 184 wherein said cell line is an NSO cell line.

339. (New) The method of claim 188 wherein said cell line is a CHO cell line.

340. (New) The method of claim 188 wherein said cell line is an NSO cell line.

341. (New) The method of claim 194 wherein said cell line is a CHO cell line.

342. (New) The method of claim 194 wherein said cell line is an NSO cell line.

343. (New) The method of claim 199 wherein said cell line is a CHO cell line.

344. (New) The method of claim 199 wherein said cell line is an NSO cell line.

345. (New) The method of claim 205 wherein said cell line is a CHO cell line.

346. (New) The method of claim 205 wherein said cell line is an NSO cell line.

347. (New) The method of claim 210 wherein said cell line is a CHO cell line.



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348. (New) The method of claim 210 wherein said cell line is an NSO cell line.

349. (New) The method of claim 217 wherein said cell line is a CHO cell line.

350. (New) The method of claim 217 wherein said cell line is an NSO cell line.

351. (New) The method of claim 218 wherein said cell line is a CHO cell line.

352. (New) The method of claim 218 wherein said cell line is an NSO cell line.

353. (New) The method of claim 219 wherein said cell line is a CHO cell line.

354. (New) The method of claim 219 wherein said cell line is an NSO cell line.

355. (New) The method of claim 220 wherein said cell line is a CHO cell line.

356. (New) The method of claim 220 wherein said cell line is an NSO cell line.

357. (New) The method of claim 221 wherein said cell line is a CHO cell line.

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358. (New) The method of claim 221 wherein said cell line is an NSO cell line.

359. (New) The mammalian host cell line according to claim 105 which is an immortalized cell line.

360. (New) The mammalian host cell line according to claim 114 which is an immortalized cell line.

361. (New) The mammalian host cell line according to claim 122 which is an immortalized cell line.

362. (New) The mammalian host cell line according to claim 130 which is an immortalized cell line.

363. (New) The mammalian host cell line according to claim 140 which is an immortalized cell line.

364. (New) The mammalian host cell line according to claim 149 which is an immortalized cell line.

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365. (New) The mammalian host cell line according to claim 159 which is an immortalized cell line.

366. (New) The mammalian host cell line according to claim 168 which is an immortalized cell line.